development of the nervous system has not previously been determined.

Thus, there exists a need to identify genes that regulate the development of the nervous system and related biological functions. The present invention satisfies this need and provides related advantages as well.

SUMMARY OF THE INVENTION

The invention provides an isolated Nope polypeptide, or functional fragment thereof, containing the amino acid sequence of a Nope polypeptide (SEQ ID NO:2), or a modification thereof. The invention also provides an isolated nucleic acid molecule encoding a Nope polypeptide amino acid sequence referenced as SEQ ID NO:2, or a modification thereof. The invention additionally provides an isolated nucleic acid molecule containing the nucleotide sequence referenced as SEQ ID NO:1, or a modification thereof. The invention further provides methods of detecting Nope polypeptides and Nope nucleic acid molecules.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the genomic localization of the Nope gene, the tissue-specific expression of Nope mRNA, and the domain structure of Nope polypeptide. Figure 1A shows the location of expressed sequence tags (ESTs) in the genomic region upstream of the Punc gene, which are shown as black bars with the corresponding Genbank accession numbers indicated. The region designated e11 is the cloned restriction fragment used to generate a Nope hybridization

probe. The Nope polyadenylation signal and the ATG start codon of the Punc gene are shown. Figure 1B shows the domain structure of the Nope protein in comparison to Neogenin, DCC, Punc, and NCAM.

Figure 2 shows the nucleotide and amino acid sequence of Nope and the nucleotide sequence of Nope genomic DNA. Figure 2A shows the nucleotide sequence of the Nope cDNA (SEQ ID NO:1). Figure 2B shows the amino acid sequence derived from cDNA clones of the Nope gene (SEQ ID NO:2), which is encoded by nucleotides 1-3756 of Figure 2a (SEQ ID NO:45). First shaded area corresponds to the signal peptide (amino acids 1-21); second shaded area corresponds to the transmembrane domain (amino acids 954-977); the first four underlined regions correspond to immunoglobulin (Ig) domains (Ig domain 1 (Ig1); amino acids 47-127)(Ig2; amino acids 155-218)(Ig3; amino acids 256-318)(Ig4; amino acids 347-411); the last five underlined regions correspond to fibronectin-type III (FnIII) domains (FnIII domain 1 (Fn1); amino acids 429-511)(Fn2; amino acids 527-609)(Fn3; amino acids 630-725)(Fn4; amino acids 750-831)(Fn5; amino acids 848-931). Figure 2C shows the nucleotide sequence of a genomic sequence (SEQ ID NO:43) encoding the 5' region of the Nope cDNA. The start codon is shown in bold, the coding region of the first exon (SEQ ID NO:44) is underlined, and the splice site is shown in italics.

Figure 3 shows the evolutionary relationships between Nope and other members of the Ig superfamily. Figure 3A shows the evolutionary relationship between Nope and the Ig superfamily. Figure 3B shows the evolutionary relationship between individual Ig domains derived from

Nope, Punc, DCC, and Neogenin. Figure 3C shows the sequence relationship between Nope and Punc as shown by dot plot analysis based on a PAM similarity matrix. Sequence similarities appear as diagonal lines.

Figure 4 shows chromosomal mapping of Nope to chromosome 9. Structures of the encoded proteins are indicated next to the chromosome sketch. Placement of Neogenin, Nope, Punc, and BAC end markers relative to framework markers D9Mit48 and D9Mit143 on chromosome 9 are shown. Distances are given in centiRays (cR). The arrangement of BAC clones and the origin of PCR products used for mapping is shown on the right.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides Nope polypeptides and encoding nucleic acids. The invention also provides methods for detecting nucleic acids encoding Nope and methods for detecting Nope polypeptides. The methods of the invention are advantageous for specifically detecting the presence of a Nope polypeptide or a nucleic acid encoding Nope in a sample.

Nope is a newly identified mouse gene located on chromosome 9. As disclosed herein, the Nope polypeptide encoded by the Nope gene contains four immunoglobulin domains and five fibronectin-type III repeats, a single transmembrane domain and a cytoplasmic domain. Nope is a new member of the immunoglobulin superfamily of cell surface proteins and has a high level of similarity to Punc and to guidance receptors such as Deleted in Colorectal Cancer